REMARKS

Claims 2, 3, 5, 7, 8, 15, and 16 are pending in the application and are at issue.

Claims 2, 3, 5, 7, 8, and 15 stand rejected under 35 U.S.C. §102(b) as being anticipated by a Brewer et al. publication (Brewer). First, the Brewer reference was cited in the Office Action of November 11, 2004 and *overcome* in Amendment "C," filed as an RCE on April 16, 2005. As stated in the Office Action of September 21, 2005, at page 2, the examiner stated:

> "The rejection of claims 2, 3, 5, 7, 8 and 11 under 35 U.S.C. 102(b) as being anticipated by Brewer et al. (1998) of record evidenced by Dorland's Illustrated Medical Dictionary (1994) is hereby expressly withdrawn in view of Applicant's persuasive argument."

The examiner has provided no reasoning with respect to reapplying this reference two years and a number of actions *after* the reference was overcome. Any reasoning presented in Amendment "C" to overcome the Brewer reference that is not repeated below, is incorporated herein by reference.

With respect to the present rejection of claims 2, 3, 5, 7, 8, and 15 under 35 U.S.C. §102(b), the examiner is directed to the MPEP §2131 stating:

> "TO ANTICIPATE A CLAIM, THE REFERENCE MUST TEACH EVERY ELEMENT OF THE CLAIM
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> 'A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.' Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)....'The identical invention must be shown in as complete detail as is contained in the ... claim.' Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an ipsissimis verbis test, i.e., identity of terminology is not required. In re Bond, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990)."

The Brewer publication fails to anticipate the present claims because each and every element of the present claims is not disclosed therein. In addition, the differences between the present claims and Brewer are nonobvious differences, thereby precluding an obviousness rejection under 35 U.S.C. §103. In fact, and as stated above, the patentability of the present claims over Brewer has previously been admitted by the examiner.

The examiner contends that the present claims are anticipated because Brewer teaches the treatment of erectile dysfunction (ED) using sildenafil in patients suffering from Parkinson's disease (PD). In particular, Brewer teaches no more than the treatment of ED in men suffering from PD. The reference teaches the use of a commercially available treatment for ED (i.e., sildenafil, VIAGRA®) in patients with "probable" PD-related impotence. Brewer found that sildenafil was effective with side effects like those found in healthy males that use sildenafil.

The Brewer reference, however, is silent with respect to treating the parasympathetic nervous system diminution that *may* lead to ED in PD sufferers. Brewer did not attempt to treat any neuropathies, nor does the cited reference suggest that the therapy could treat a neuropathy. Brewer merely teaches treatment of a symptom, i.e., ED, of a neuropathy that "is reported in 40-60% of patients with" PD. Importantly, Brewer fails to teach or suggest treating a claimed neuropathy in an individual that is *not* suffering from ED.

Although PD is a neurological malady, it occurs in the *central nervous system*, *not* in the *periphery*. Accordingly, PD does not correspond with the symptoms and conditions associated with an autonomous or peripheral polyneuropathy, such as in the case of diabetes or the other neuropathies recited in the claims. U.S. Patent No. 5,753,225, cited by the examiner, also teaches that PD is a central nervous system disorder (column 2, lines 7-20). Accordingly, treatment of ED in patients suffering from PD is unrelated to using a presently claimed compound to treat a presently claimed neuropathy that differs from PD.

In summary, it is submitted that Brewer fails to anticipate the present claims and fails to render the present claims obvious. Brewer's teachings are limited to treating ED in males suffering from PD, which is a *central nervous system* disorder. The reference is *silent* with respect to *treating any* neuropathy, let alone a neuropathy as presently claimed, which differ from PD. Brewer also provides no disclosure that would lead a person skilled in the art to use sildenafil to treat a *neuropathy*, as presently recited in claim 5. A skilled person would read no more into the Brewer reference than a successful treatment of ED, using a known, commercial compound for treating ED, in a subset (40-60%) of males who suffer from PD and have ED as a symptom. Brewer teaches treating of this symptom, i.e., ED, but not the underlying neuropathy. Also, as stated above, the underlying neuropathy in Brewer is PD, which is a *central* nervous system disorder that is different from a presently-claimed neuropathy. Accordingly, it is submitted that this rejection of claims 2, 3, 5, 7, 8, and 15 under 35 U.S.C. §102(b) is in error and should be withdrawn. In addition, the difference

between the present claims and Brewer are substantial differences such that claims 2, 3, 5, 7, 8, and 15 would not have been obvious over the Brewer reference under 35 U.S.C. §103.

Claims 2, 3, 5, 7, 8, 15, and 16 stand rejected under 35 U.S.C. §103 as being obvious over Doherty, Jr. et al. U.S. Patent No. 6,037,346 ('346) in view of de Tejada U.S. Patent No. 6,277,884 ('884). This rejection is based on a contention that the '346 patent teaches a method of treating ED using sildenafil, that ED has been identified as "neurogenic associated with neuropathy caused by diabetes," and that the '884 patent teaches that sexual dysfunctions are attributable to neuropathy. The examiner then apparently attempts to show that treating ED with sildenafil is equivalent to treating a neuropathy with sildenafil. Applicants traverse this rejection.

The entire '346 patent is directed to the treatment of ED using a known PDE5 inhibitor and ED treatment drug, i.e., sildenafil, by a local administration of the drug. In the background of the '346 patent, impotence, impotence treatments, and impotence causes are discussed for example, at column 1, lines 21-64, stating (with citations omitted):

> "Impotence is the consistent inability to achieve or sustain an erection of sufficient rigidity for sexual intercourse. It has recently been estimated that approximately 10 million American men are impotent... Impotence is recognized to be an age-dependent disorder, with an incidence of 1.9 percent at 40 years of age and 25 percent at 65 years of age... In 1985 in the United States, impotence accounted for more than several hundred thousand outpatient visits to physicians... Depending on the nature and cause of the problem, treatments include psychosexual therapy, hormonal therapy, administration of vasodilators such as nitroglycerin and α-adrenergic blocking agents ("α-blockers-"), oral administration of other pharmaceutical agents, vascular surgery, implanted penile prostheses, vacuum constriction devices and external aids such as penile splints to support the penis or penile constricting rings to alter the flow of blood through the penis.
>
> A number of causes of impotence have been identified, including vasculogenic, neurogenic, endocrinologic and psychogenic. Vasculogenic impotence, which is caused by alterations in the flow of blood to and from the penis, is thought to be the most frequent organic cause of impotence. Common risk factors for vasculogenic impotence include hypertension, diabetes, cigarette smoking, pelvic trauma, and the like. Neurogenic impotence is associated with spinal-cord injury, multiple sclerosis, peripheral neuropathy caused by diabetes or alcoholism and severance of the autonomic nerve supply to the penis consequent to prostate surgery. Erectile dysfunction is also associated with disturbances in endocrine function resulting in low circulating testosterone levels and elevated prolactin levels.

> Impotence can also be a side effect of various classes of drugs, in particular, those that interfere with central neuroendocrine control or local neurovascular control of penile smooth muscle."

The '346 patent therefore discloses *several* causes of impotence, but the reference is directed *only* to the treatment of ED that results from these causes. There is absolutely no teaching or suggestion in the '346 patent that sildenafil is useful in treating *any* of causes of impotence, e.g., vasculogenic, neurogenic, endocrinologic, or psychogenic. A person skilled in the art would not consider using sildenafil to treat any of these underlying causes of ED not only because the '346 patent fails to teach or remotely suggest any such use, but because they are so diverse.

Although the '346 patent states that ED is associated with peripheral neuropathy caused by diabetes and alcoholism, the reference is limited to teaching the treatment of ED, not the underlying condition. The reference contains no teachings or suggestions that a peripheral neuropathy would respond favorably to sildenafil. Furthermore, sildenafil activity is related to PDE5 inhibition. Phosphodiesterase inhibitors have not been implicated in the pathogenesis of peripheral neuropathy, thus a person skilled in the art would not even consider using a PDE5 inhibitor, e.g., sildenafil, to treat a presently claimed neuropathy. Further, where in the '346 patent would a person skilled in the art receive the incentive to make a drastic jump in reasoning and treat an individual *not* suffering from ED with sildenafil in order to treat an underlying condition that causes the ED? From the numerous underlying conditions that cause ED recited in the '346 patent, the skilled person then would have to select treating a claimed neuropathy, even though PDE5 inhibition has not been linked to the claimed neuropathies.

The effect of sildenafil upon a peripheral polyneuropathy was unexpected and the present disclosure is first to report this effect. The mere indication in the '346 patent that erectile dysfunction is a symptom of polyneuropathy, i.e., the autonomous nervous system, does not lead to the conclusion that sildenafil is effective in the treatment of peripheral neuropathy.

The '884 patent does not overcome the deficiencies of the '346 patent. The '884 patent is directed to the treatment of sexual dysfunction using N-hydroxyguanidine compounds. The disclosed compounds stimulate the production of nitric oxide, and

therefore, perform differently from sildenafil, which is a PDE5 inhibitor (although a result of PDE5 inhibition is an indirect increase in nitric oxide).

The '884 patent teaches that the disclosed compounds can be used to treat hypoxic conditions, including *central* nervous system disorders. Notably no peripheral neuropathies were disclosed. The examiner relies upon column 3, lines 15-20 of the '884 patent stating that the sexual dysfunction can be attributable to neuropathy.

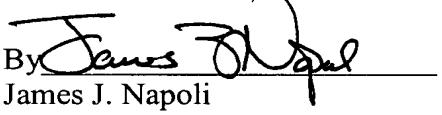
However, like the primary '346 patent, the '884 patent fails to teach or suggest treating an underlying cause of ED. The reference teaches that other conditions can be treated by the disclosed compounds. See '884 patent, column 3, lines 28-37. These conditions do not include the neuropathies recited in the present claims. Accordingly, the '884 patent fails to add any information to the '346 disclosure, and in fact is directed to a different class of compounds that act by a different mechanism.

In summary, the combination of the '346 and '884 patents merely teaches compounds and methods of treating ED, and that ED may be caused by a neuropathy. The references, alone or in combination, fail to teach or suggest treating *any* of the numerous underlying conditions that cause ED, let alone the peripheral neuropathies presently recited in the claims. Accordingly, it is submitted that claims 2, 3, 5, 7, 8, 15, and 16 would not have been obvious over a combination of the '346 and '884 patents, and that the rejection of these claims under 35 U.S.C. §103 should be withdrawn. An early and favorable action on the merits is respectfully requested.

Should the examiner wish to discuss the foregoing, or any matter of form in an effort to advance this application toward allowance, the examiner is urged to telephone the undersigned at the indicated number.

Dated: May 25, 2007

Respectfully submitted,

By 

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